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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,578	11/16/2005	David A Sanders	290.00500101	5513

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EXAMINER	
PENG, BO	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
11/25/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,578	SANDERS ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-9,11 and 13* is/are pending in the application.

4a) Of the above claim(s) *3,4,7 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,8,9,11 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/22/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office action is in response to the amendment filed July 22, 2009. Claims 5, 10, 14-25 have been cancelled. Claims 1-4, 6-9, 11, 13 are pending. Claims 3, 4, 7 and 12 have been withdrawn as non-elected. Claims 1, 2, 6, 8, 9, 11 and 13 are considered in this Office action.

Claim Rejections - 35 USC § 112, second paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. **(Prior rejection-moot)** The rejection of Claim 10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is moot in view of the cancellation of the claim.

4. **(New rejection necessitated by the amendment)** Claims 1, 2, 6, 8, 9, 11 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 1, 9 and 13 recites: "... an Ebola glycoprotein containing a deletion of amino acids 309 to 489 in SEQ ID NO: 1". First, SEQ ID NO:1 is a nucleic acid sequence, not an amino cid sequence. The "amino acids 309 to 489 in SEQ ID NO: 1" cited in the claims are not corresponding to the nucleic acid of SEQ ID NO:1. Appropriate correction is required. This rejection affects all dependent claims.

Claim Rejections - 35 USC § 112, first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. **(Prior rejection-maintained)** The rejection of Claims 1, 8 and 13 under 35 U.S.C. 112, first paragraph, as failing to comply with written description requirement, **is maintained** for the reason of record.

In response to Applicant's argument:

8. Applicant asserts that claims 1 and 13 are amended herewith to delete recitation of "a glycoprotein comprising a modified O-glycosylation region" and recite in its place "an Ebola glycoprotein containing a deletion of amino acids 309-489 of **SEQ ID** NO:1 in the O-glycosylation region." Applicant asserts that the amendment has overcomes the rejection.

9. This argument is not persuasive. First, the amendment of "an Ebola glycoprotein containing a deletion of amino acids 309-489 of SEQ ID NO:1" is an error, see Para 5 above.

10. More important, as indicated in the previous Office action, the specification has not provided adequate description indicating *which* are claimed subgenus retroviruses pseudotyped with modified GPs that have transduction efficiency at least 2-fold higher than those with the wild-type GP in a genus of retroviruses pseudotyped with any modified GPs in *O*-glycosylation region; See Para 12-16 Applicant has not addressed this issue. The rejection is maintained for the same reason of record.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. **(Prior rejection-withdrawn)** The rejection of Claims 1, 2, 6, 9 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang *et al.* (Nature Medcine, 6(8):886-889, cited in IDS), as evidenced by Yang S. (Hum Gene Ther. 1999 Jan 1;10(1):123-32), **is withdrawn** in view of the amendment to the claims.

13. **(Prior rejection-withdrawn)** The rejection of Claims 1, 2, 6, 9 and 11 under 35 U.S.C. 102(a) as being anticipated by Simmons *et al.* (J. Virology, 76(5):2518-2528, March, 2002, cited in IDS), in view of Wood-Lewis (J. Virology, 72(4): 3155-3160, cited in IDS) and Soneoka Y *et al.* (Nucleic acid Res. 1995, Vol. 23(4):628-633), **is withdrawn** in view of the amendment to the claims.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. **(Prior rejection-maintained)** The rejection of Claims 8 and 13 under 35 U.S.C. 103(a) as being unpatentable over either Yang or Simmons, as applied in Claims 1, 2, 5, 6, 9 and 11 above, further in view of Wood-Lewis, **is maintained** and is restated necessitated by the amendment as set forth below

16. Claims 1, 2, 6, 8, 9, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang *et al.* (Nature Medcine, 6(8):886-889, cited in IDS), Yang S. (Hum Gene Ther. 1999 Jan 1;10(1):123-32), Simmons *et al.* (J. Virology, 76(5):2518-2528, 2002, cited in IDS), and Wood-Lewis (J. Virology, 72(4): 3155-3160, cited in IDS) and Soneoka Y *et al.* (Nucleic acid Res. 1995, Vol. 23(4):628-633).
further in view of Wood-Lewis,

17. Yang teaches a pseudotyped murine leukemia virus (MLV, also called as Mo-MuLV) with Ebola virus GP(Δmuc) comprising deletion of a mucin-like domain of **amino acids 315-505**, see e.g. line 2-10, right col. p. 886, and Para 2, right col. p. 889. Yang's MLV pseudotyped with Ebola GP inherently comprises an MLV core, in view of Yang S (1999) cited as Ref #15 in Yang. Yang S (1999) teaches the DNA constructs encoding MLV core (see Fig. 1), which encodes "recombinant RNA comprising (i) a nucleotide sequence GFP (a selected biomolecule intended for delivery to a target cell), and (ii) retroviral control elements for packaging, reverse transcription and integration of the retrovirus into a target cell, see e.g. Fig. 1.

18. Simmons teaches a pseudotyped murine leukemia virus (MLV) with Ebola virus GP (filovirus GP) comprising deletion of an *O*-glycosylation region of **amino acids 311-463**, Fig. 3A. Simmons' pseudotyped MLV with Ebola GP inherently comprises the

MLV core, in view of Wood-Lewis (cited as ref #48 in Simmons) and Soneoka (cited as Ref #26 in Soneoka). Wood-Lewis teaches the source of the MLV packaging system; see Para 4, left col. p. 3156. Soneoka teaches the DNA constructs encoding the MLV core (see Fig. 1), which encodes "recombinant RNA comprising (i) a nucleotide sequence lacZ (a selected biomolecule intended for delivery to a target cell), and (ii) retroviral control elements for packaging, reverse transcription and integration of the retrovirus into a target cell, see e.g. Fig. 1.

19. However, neither Yang nor Simons explicitly teaches that deletion of amino acids 309-489 of Ebola GP, nor the pseudotyped MLV with a modified Ebola GP has a transduction efficiency into a target cell at least 2-fold higher than a retrovirus pseudotyped with the wild-type GP.

20. It would have been obvious to one of ordinary skill in the art at the time the invention was made to make of a pseudotyped MLV with Ebola virus GP (filovirus GP) comprising deletion of an *O*-glycosylation region of amino acids 309-486. The skilled artisan would have been motivated to do so because both Yang and Simons have show that deletion of an *O*-glycosylation region of Ebora virus GP reduces cell cytotoxicity and cell injury. There would have a reasonable expectation of success that deletion of that deletion of amino acids 309-489 of Ebola GP would work for gene transfer, because Yang and Simons have shown that the pseudotyped MLV with modified Ebola GP comprising a deletion of either amino acids 315-505 or amino acids 311-467 can be used for gene transfer and with reduced GP toxicity to host cells. In other words, deleting amino acids 309-489 appears to be design choice. Moreover, it was routine practice in a lab to characterize transduction efficiency into target cells, as evidenced by Wood-Lewis.

Wood-Lewis teaches characterizing transduction efficiency of MLV pseudotyped with Ebola GP in a variety of target cells, see e.g. bridge paragraph between left col. and right col. p. 3157, and Table 1. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

In response to Applicant's argument:

21. Applicant argues that deletion of amino acids 309-489 from Ebola glycoprotein unexpectedly resulted in a modified glycoprotein that, when used for pseudotyping, significantly increases transduction efficiencies. See, e.g., the specification at page 19, lines 11-12, wherein the Applicants state that **"[r]emarkably, processing and viral incorporation of the A309-489 GP was greatly enhanced as shown in Figure 2"** and page 19, lines 27-28, "[t]he effect of deleting the O-glycosylation region of GP1 (A309-489) on expression and transduction were striking."

22. This argument is considered but found not persuasive. The specification [0015] recites: [0015] FIG. 2 is a western blot showing the expression and incorporation of the Δ308-489 Ebola GP into pseudotyped retrovirus. Fig. 2 shows that MLV containing deletion of amino acids 309-489 from Ebola glycoprotein has different protein sizes, see Fig. 2. This result is expected by one of ordinary skill in the art because deletion of 180 amino acids (amino acids 308-489) would reduce the size of the protein compare to the wild type GP without the deletion. There is no factual evidence in the specification that how "[t]he effect of deleting the O-glycosylation region of GP1 (A309-489) on expression and transduction were striking." Therefore, Applicant's argument of "unexpected result" is not persuasive.

Remarks

23. No claim is allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648